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EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/698,794	PAULETTI ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59-86* is/are pending in the application.

4a) Of the above claim(s) *70-72 and 77-86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-69, and 73-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response, filed 03/30/09, has been fully considered and made of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is final. The finality of the action is necessitated by the amendment of the claim narrowing the scope of the claims (i.e. by the recitation of the term "wherein at least 55% of said therapeutic agent is released from said film within two hours").

Status of the Claims

Claims 59-86 are currently pending in this application.

Claims 70--72, 77-86 are withdrawn for being directed to non-elected subject matter.

Claims 59-69, 73-76 are under examination.

Election of Species

It is noted that the election requirements regarding the application of films or foams (e.g. use as a coating, tampon, pessary, suppository, pad, strip ,cyclinder, sphere, or beads), and the election requirement regarding (see Office action, mailed 12/21.06, page 5) are withdrawn for examination purposes. The restriction/election requirements as amended herein are made final.

REJECTION

NEW MATTER REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

Claims 59-69, 73-76 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 59 recites the term "consisting essentially of." However, applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art as the instant disclosure provides support for exclusion of other active ingredients from the claimed polymer film formulation as evidenced by the fact that dependent claim 65, for example, recites the term "further comprising," which reasonably contemplates the inclusion of additional active ingredients in the instant claimed polymer film formulation. Besides, applicant has not provided any evidence to show that inclusion of additional components in the claimed formulation would materially affect the basic and novel characteristics of the instant claimed invention (MPEP 2111.03). For example, applicant discloses that other additional excipients and additives can be included in the composition (specification, pages 31-32).

Dependent claims 60-69 and 73-76 are rejected for the same reason as these claims fail to correct the deficiency of the claim from which they depend (i.e. claim 1).

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that applicant was in

possession of the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the criticality of excluding the addition of other active ingredients to the film formulation.

Thus, claims 59-69 and 73-76 are rejected for introduction of new subject matter.

Response to applicant's arguments

Applicant's arguments with respect to the rejection under 112, 2nd paragraph have been considered but are moot in view of the new ground(s) of rejection

Claim rejections – 35 USC 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 65, 67, 69, and 73-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 59 recites the term "consisting essentially of," while dependent claims 65, 67, 69, 73, and 74 recite the term "comprising." Since the terms "consisting essentially of" and "comprising" have contradictory meanings, one of skill in the art would not be able to reasonably determine the metes and bounds of the claimed

subject (see MPEP 2111.03). Hence, claims 65, 67, 69, 73, and 74 are found to be indefinite.

Also, claims 59-69, 73-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular claim 59 recites the term "prepared from an evaporated solution consisting essentially of a therapeutic agent, a substrate polymer, a penetration enhancer, a surfactant and plasticizer." This renders the claimed subject indefinite because it is not clear how the film "consisting essentially of a therapeutic agent, a substrate polymer, a penetration enhancer, a surfactant and plasticizer" can be formed after the solution "consisting essentially of a therapeutic agent, a substrate polymer, a penetration enhancer, a surfactant and plasticizer" is evaporated even though it appears that said film is formed following the evaporation of only the solvent (e.g. water).

Dependent claims 60-69, and 73-76 are rejected for the same reason because these claims fail to correct the deficiency from which they depend.

Response to applicant's arguments

Applicant's arguments with respect to the rejection under 112, 2nd paragraph have been considered but are moot in view of the new ground(s) of rejection.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 59 is rejected under 35 U.S.C. 103(a) as being unpatentable over Virgalitto et al. (US Patent Application Pub. No. 2005/0089548 A1), in view of Elsohly et al. (US Patent Application Pub. No. 2006/0257463 A1).

The rejection under 112, 2nd paragraph is noted. For purposes of this rejection

the term "consisting essentially of" is being construed to mean "comprising." Further, applicant has not provided any evidence to show that inclusion of additional components as taught by the prior art would materially affect the basic and novel characteristics of the instant claimed invention (MPEP 2111.03).

Virgalitto et al. (US Patent Application Pub. No. 2005/0089548 A1) teach edible films that contain an active substance, for example, a flavorant, fragrance, pharmaceutical or nutraceutical, or mixtures thereof (para. 0001). Virgalitto et al. state that edible film is useful for delivering pharmaceuticals, particularly in patients who have difficulty swallowing conventional oral dosage forms (para. 0002). Virgalitto et al. disclose that addition of active agents directly to the film forming ingredients may influence the film's physical properties or may introduce process constraints in the films manufacture that may add complexity, duration and cost to the film making process (para. 0007). Virgalitto et al. state that there is a need for edible film that can reliably retain an active agent with a high loading, in particular a flavor or fragrance material during processing and storage and which is mechanically robust to withstand long periods of storage, and handling (para. 0008). Virgalitto et al. disclose that it is desirable to provide a film which also disintegrates, disperses or dissolves rapidly to release its active agent on demand, for example, when placed on a food product during cooking, or when placed directly in or on the human body, e.g. in the oral cavity, without causing adverse mouth feel (para. 0008). Virgalitto et al. teach formulations that provide the formulator with considerable latitude to effect release of different active agents on

demand, in a time-dependent manner (para. 0014). Virgalitto et al. teach that any known hydrocolloid film forming material can be used for their film-forming properties in the food industry, or the pharmaceutical industry; any film-forming material that is capable of rapidly hydrating, and dispersing or dissolving in water may be employed (para. 0023). Virgalitto et al. teach preferred film-forming materials, including chemically or physically modified starches, alginates (e.g. sodium alginate), pectins, tragacantha, acacia gum, gum arabic, agar, gelatin ..., cellulose polymers (e.g. hydroxypropylmethyl cellulose), ..., and mixtures thereof; para. 0023). Virgalitto et al. disclose that the materials are chosen for their ability to rapidly hydrate, and disperse or dissolve on a substrate to which they are applied, or in the oral cavity and that preferred materials dissolve or disperse in the oral cavity, or on food to which they are applied within about 20 seconds to release the active agent contained in the film, and present the encapsulated active agent thereby to deliver a sustained release active agent (para. 0024). Virgalitto et al. teach that alginates are particularly preferred film-forming materials (para. 0026). Virgalitto et al. teach that hydrocolloid film-forming material may be employed in varying amounts depending on the nature of the material, the particular film-forming conditions employed, the desired properties of the edible film, and the nature of the other ingredients employed in the film (para. 0027). However, for most purpose, high amounts of the film-forming material is desirable e.g. from 50 to 90% by weight of the total solids of the film-forming composition (para. 0027). Virgalitto et al. teach that synthetic polymers, soluble or swellable in water, may also be employed, for example, polyvinylpyrrolidone, polyvinyl alcohol, polyacrylic acid, or polyacrylamide

(para. 0023). Virgalitto et al. state that other optional ingredients may include preservatives and anti-microbial agents as are commonly employed in foodstuffs, nutrient formulations, and pharmaceuticals (para. 0022). Also, Virgalitto et al. state that the edible film may contain other optional ingredients that may confer additional benefits or properties on the film (para. 0018). Virgalitto et al. teach films that may be provided in continuous sheets (para. 0076). Virgalitto et al. state that the thickness of the films can be precisely controlled during the manufacturing process to vary, for example, between 5 and 200 microns (para. 0077). In addition, Virgalitto et al. state that the amount of pharmaceutical ... agent employed will depend upon the particular condition to be treated and the particular active agent employed as will be appreciated by the skilled person (para. 0068).

However, Virgalitto et al. do not teach polyethylene oxide polymer (= applicant's elected polymer species) and is silent regarding the amount of active pharmaceutical agent that can be employed in the film (para. 0068).

Elsohly et al. (US Patent Application Pub. No. 2006/0257463 A1) transmucosal device film or films (in the case of co-extrusion or layering = film sheet) comprising at least one water-soluble, water-swellable or water-insoluble thermoplastic **polymer** such as, but not limited to, hydroxypropycellulose, polyethylene oxide, ..., and hydroxymethyl cellulose); one or more cannabinoid medicaments (= therapeutic agent); a bioadhesive, such as water-soluble or water swellable polymers derived from acrylic acid or a pharmaceutically acceptable salt thereof, including polyacrylic acid polymers (e.g.

carbomers, polycarbophils and/or water-soluble salts of a cop-polymer of methyl vinyl ether and maleic acid or anhydride); one or more **pH adjusting agents** to improve stability and solubility (e.g. potassium metaphosphate, potassium phosphate, monobasic sodium acetate and sodium citrate anhydrous and dehydrate, ethanolamine, sodium borate, sodium carbonate, sodium bicarbonate, sodium hydroxide); and other additives, including **penetration enhancers**, and/or hydrophobic polymers, cross-linking agents to, for example reduce matrix erosion time (e.g. an organic acid such as tartaric acid, alpha-hydroxy acid, citric acid, fumaric acid, succinic acid), to render the film useful for transmucosal application (para. 0021-0039). Elsohly et al. teach that the transmucosal preparation may also contain other components that modify the extrusion, molding, or casting characteristics or physical properties of the matrix, including, for example, **polyethylene**, xylitol, sucrose, surface-active agents, ..., and combinations thereof (para. 0026). Elsohly et al. teach transmucosal preparations may comprise super-disintegrants or absorbents e.g. sodium starch glycolate (Explotab or Primojel), croscarmellose sodium (Ac-Di-Sol), cross-linked PVP (Polyplasdone XL 10), clays, alginates, corn starch, potato starch, pregelatinized starch, modified starch, cellulosic agents, ..., gums,..., and other disintegrants known to those of ordinary skill in the art (para. 0027); transmucosal preparation may also contain an antioxidant (e.g. **sodium metabilsulfate**, sodium bisulfite, **vitamin E and its derivatives**), chelating agent (e.g. EDTA, polycarboxylic acids, polyamines, and derivatives thereof), stabilizer, **surfactant** (e.g. sucrose stearate, vitamin E deriviatives, sodium lauryl sulfate, dioctyl sodium sulfosuccinate), preservative (e.g. methyl paraben) , ..., flavor, colorant,

fragrance and combinations thereof (paras. 0028-0039). Elsohly et al. teach that transmucosal preparations that provide a controlled release of an agent, wherein said preparation contain a suitable release rate modifier, wherein said suitable **release rate modifier** include: poly (ethylene oxide) or PEO; hydroxypropyl methylcellulose (HPMC); ..., polycarbophil, carbomer or a polysaccharide (para. 0038). Elsohly et al. teach that preferably said transmucosal formulations comprise a **penetration enhancer**, which may also be referred to as an absorption enhancer or permeability enhancer, which may include bile salts (e.g. sodium deoxycholate), **surfactants** (e.g. sodium lauryl sulfate, polysorbate 80, laureth-9, benzalkonium chloride, cetyl chloride, and polyoxyethylene monoalkylethers), benzoid acids (e.g. sodium salicylate, methoxy salicylate), fatty acids (e.g. lauric acid, oleic acid, undecanoic acid and methyl oleate), fatty alcohols (e.g. octanol, nonanol), laurocapram, polyols (e.g. propylene glycol, glycerin), cyclodextrins, sulfoxides (e.g. dimethyl sulfoxide and dodecyl methyl sulfoxide), terpenes (e.g. menthol, thymol, and limonene), urea, chitosan and other natural and synthetic polymers; polyoxyethylene monoalkylethers include Brij® and Myrj® series (paras. 0016 , 0033). Elsohly et al. teach a method for increasing the permeability of a patient's mucosa by including a permability enhancement agent in the transmucosal formulation, wherein said permeability enhancement agent is PEG 400, and/or other enhancers in which cannabinoids may be solubilized; useful solubilizers which may inherently be penetration or absorption enhancers, include, for example, polyethylene glycol (PEG), propylene glycol, Dibutyl subacetate, Glycerol, Diethyl phthalate (phthalate esters), triacetin, citrate esters-triethyl citrate (TEC), acetyltriethyl

citrate (ATEC), tributyl citrate (TBC), acetyltributyl citrate (ATBC), benzyl benzoate, sorbitol, xylitol, Miglyol (glycerides), bis(2-ethyllhexyl) adipate, mineral oil, polyhydric alcohols such as glycerin and sorbitol, glycerol esters such as glycerol, triacetate; fatty acid triglycerides such as NEOBEE* M-5 and mineral oil, vegetable oils such as castor oil, etc., polyoxyethylene sorbitan, fatty acid esters such as TWEENS, polyoxyethylene monoalkyl ethers such as **BRIJ** and MYRJ series, sucrose monoesters, lanolin esters, lanolin ether, and **chitosan** and other natural and synthetic polymers (paras. 0014-0016). Also included as solubilizers for the cannabinoids are organic solvents, such as ethanol, benzene and the like, which may be utilized in solvent cast techniques (para. 0014). Elsohly et al. exemplify transmucosal formulations comprising polyethylene oxide (PEO i.e. applicant's elected polymer species) in amounts ranging from **10%-80.4%** (para. 0043-0053, including Examples 2-6, and Tables I and III). Elsohly et al. also **exemplify transmucosal formulations** comprising PEO (10-13%; i.e. polymer substrate), PEG 400 (8-12%; i.e. absorption enhancer/solubilizer/penetration enhancer), citric acid (0.5%), sodium dexoycholate (5% = permeability enhancer/penetration enhancer), methyl paraben (0.2%), **THC (8-16% = therapeutic agent = anti-migraine/non-steroidal anti-inflammatory agent/anti-nausea agent**), hydroxypropyl cellulose (55.23-63.23%), polyvinylpuyrrolidone 10%, butylated hydroxyl toluene (0.05%), and carbomer (5%). See page 6, para 0051, Table 1). Elsohly et al. (US Patent Application Pub. No. 2006/0257463 A1) teach methods for preparing transmucosal formulations via, for example, hot-melt extrusion, hot-melt molding, by admixing or utlilizing a solvent cast technique, and wherein an effective amount of a

cannabinoid is incorporated into the transmucosal cannabinoid-containing preparation, and wherein said transmucosal formulation include a matrix patch for retaining and dispersing the active ingredients (para. 0015). Elsohly et al. teach formulations comprising a bioadhesive system that is an effective, feasible, and convenient intra-oral drug delivery system for applying and delivering controlled dosages of cannabinoids through or into the oral cavity, which may also be extended top controlled drug delivery in gynecological (vaginal), nasal, sinus, and ophthalmic applications (para. 0019). Elsohly et al. teach single and multi-layered laminated (= sheet) film matrix containing cannabinoids, wherein said matrix can be cut or formed into almost unlimited shapes and sizes, depending on the application and dosage intended (para. 0020). In addition, Elsohly et al. teach that cannabinoids (i.e. non-steroidal anti-inflammatory agents) have various **medicinal uses**, including treatment of nausea (= anti-nausea agent), pain, migraines (i.e. anti-migraine agent), and rheumatic (i.e. anti-inflammatory effect) and osteo-arthritis (i.e. anti-inflammatory effect), muscle dysfunction associated with multiple sclerosis. (para. 0006). Elsohly et al. also exemplify transmucosal formulations comprising vitamin E TPGS (=α-tocopherol polyethylene glycol succinate; see para. 0048, Examples 5 and 6). Also, Elsohly et al. exemplify formulations comprising polyethylene oxide in an amount of 68% and a pharmaceutical active agent (THC) in an amount of 8% and (= calculated ratio amount of 76:1).

It would have been obvious to a person of skill in the art at the time the invention was made to combine the teachings of the cited references by selecting any suitable soluble or swellable polymer to optimize the release properties of the edible film

compositiom, including arriving at the instant claimed invention, depending on the particular active agent and end use of the product (para. 0007). One would have been motivated to do because Virgalitto et al. suggest that the formation of edible films poses a considerable technical challenge that the prior art does not address and that it is desirable to provide films that disintegrate, disperses, or dissolves rapidly to release its active agent on demand, for example, when placed directly in or on the human body (e.g. oral cavity; para. 0008) and Esohly et al. teach transmucosal polymer film drug delivery systems for intra-oral and vaginal applications (para. 0018), wherein said polymer film may comprise of various polymers, including polyethylene oxide (PolyOx), polyvinylpyrrolidone (Kolidon), hydroxypropyl cellulose (Klucel), ..., alginates, alginic acid; and wherein said film matrix may optional contain a bioadhesive such as carbopol, polycarbophil, chitosan, ort others known in the art (paras. 0009 and 0019). Besides, Virgalitto et al. teach films that provide many advantages with respect to stability and active drug delivery, including delivering active fragrances that mask undesirable odours (para. 0011) such that one would reasonably expect to modify the film composition of Virgalitto et al. in view of Elsohly et al. to optimize the vaginal ordour masking effect of the formulation since Virgalitto et al. suggest film formulations for application to any part of the body (e.g. oral cavity; para. 0008) and Elsohkly teach film formulations that may be applied to various body parts, including the oral cavity and vagina (= applicant's elected epithelium species; para. 0022). Beside, both references are directed formulations comprising fragrances.

It is noted that the instant claims are directed to a product and not a method of using or making a product.

Regarding the substrate polymer limitation of claim 59, Virgalitto et al. teach edible film for application directly in or on the human body (e.g. oral cavity; para 0008), wherein said film may be formed from any hydrocolloid film forming material that is capable of rapidly hydrating and dispersing or dissolving in water, and further wherein the preferred film-forming material includes, for example, alginates (e.g. sodium alginate), and cellulose polymers (e.g. hydroxypropylmethyl cellulose; para 0023).

With respect to the term "present in from about 2% to about 100%, by weight," Virgalitto et al. teach high amounts of the film-forming material is desirable, for example, from 50 to 90% by weight of the total solids of the film forming composition (para. 0027).

Regarding the therapeutic agent limitation of claim 1, Virgalitto et al. teach edible film delivery systems for delivery of active ingredients, including pharmaceutical agents (e.g. anti-inflammatory drugs paras. 0043 and 0067), which overlaps with the instant claimed therapeutic agents.

With respect with the term "present in an amount from about 0.1 to about 2000 mg.," Virgalitto et al. teach that the amount of the pharmaceutical agent employed will depend upon the particular condition to be treated and the particular agent employed as well, which will be appreciated by the skilled person. Hence, it is the examiner's position that it would have been within the scope of knowledge and skill of the artisan at the time the invention was made to employ any suitable dose of the therapeutic agent (e.g. anti-inflammatory agent), including applicant's claimed dosage amount, depending on the

specific anti-inflammatory agent and the particular condition/severity of condition treated with said agent since it is routine the art to manipulate the dose amounts of therapeutic agents depending on the end use of the pharmaceutical formulation.

Regarding the penetration enhancer limitation recited in claim 59, Virgalitto et al. teach emulsifiers (e.g. glycerides, oleates) in amounts of up to 2% by weight and the instant claim recites, for example, the term "wherein saind penetration enhancer is selected from the group consisting of ..., glyceride, ..., present in from about 0.1% to about 60%, by weight," which overlaps with the teaching of the prior art such that one would reasonably expect that films comprising glyceride in an amount of up to 2% as taught by Virgalitto et al. would reasonably exhibit the instant claimed penetration enhancing properties as well.

Regarding the plasticizer limitation of claim 59, Virgalitto et al. teach that plasticizers (e.g. glycerol = glyceim, polyethylene glycol, propylene glycol, sorbitol; para. 0072) may be employed in the edible film in amounts of up to 5% (para. 0073), which overlaps with the term "wherein said plasticizer is selected from the group consisting of glycerin, ..., present in from about 5% to about 25%, by weight."

Regarding the surfactant limitation of claim 59, Virgalitto et al. teach emulsifiers (e.g. non-ionic surfactants), wherein said emulsifiers may be employed in an amounts of up to 2% by weight (paras 0070-0071). Further, it is noted that the term "a non-ionic surfactant (Brij)" as recited in claim 59 is considered to encompass the genus of non-ionic surfactants and therefore is not limited to "Brij," which is considered to represent an example of a non-ionic surfactant.

Regarding the term "wherein said film is prepared as a single or double sided solid or semi-solid film strip, ..., film sheet, or as a liquid preparation that forms a film layer upon contact with an epithelial tissue or with a surface of non-film device made of different material" as recited in claim 59, it is noted that Virgalitto et al. exemplify film strips (Figures 2-3, and paras. 0074, and 0076-0077).

Regarding the term "wherein at least 55% of said therapeutic agent is released from said film within two hours onto a vaginal, nasal, buccal, scrotal or labial epithelium and delivered through said epithelium into systemic circulation," it is noted that Virgalitto et al. teach edible film that quickly hydrate and is softened and develops mucoadhesive properties, wherein thereafter said film disperses or dissolves rapidly in the oral cavity, wherein the effect of the film last for 20 minutes or more (para. 0078; see also para 0024) such that one would reasonably expect that at least 55% of the therapeutic agent to be released from the film within hours in view of the fact the edible film rapidly disperses/dissolves when placed in contact with body cavities (e.g. oral cavity and vagina) since these cavities secrete fluids (i.e. saliva and vaginal fluids) capable of dissolving said swellable polymer. Further, since the prior art teaches every claim limitation, the prior art is considered to be capable of performing the intended function, including delivering the therapeutic agent through the epithelium into the systemic circulation as claimed.

With respect to the preamble, Virgalitto et al. teach an edible polymer film that can be placed in or on the human body (e.g. oral cavity) and the oral cavity is comprised of an oral mucosa such that placement of the edible polymer film in the oral cavity would

be expected to serve as a topical transmucosal delivery system for the therapeutic agent therein.

Thus, one would have deemed it obvious to create the instant claimed invention with reasonable predictability.

Claims 60-69 amd 73-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Virgalitto et al. (US Patent Application Pub. No. 2005/0089548 A1), in view of Elsohly et al. (US Patent Application Pub. No. 2006/0257463 A1), in further view of Harrison et al. (US Patent 6,086,909).

The above discussions of Virgalitto et al. and Elsohly et al. are incorporated by reference.

However, these references do not teach applicant's elected active agent species (ketorolac).

Harrison et al. teach methods of treating dysmenorrhea comprising applying a drug delivery sytstem direcity to the uterus via the vaginal mucosa, wherein said drug delivery system comprises a pharmaceutical agent preferably selected from the group consisting of, for example, non-steroidal anti-inflammatory drugs (NSAIDS; col. 7, lines 26-39); and wherein the preferred NSAIDs include, for example, ketorolac (col. 7, lnes 51-67).

It would have been obvious to a person of skill in the art to add any suitable therapeutic agent (e.g. ketorolac) as taught by Harrison et al. (col. 6, line 6 to col. 8, line 22) to the film formulation encompassed by the prior art for its anti-inflammatory

properties. One would have been motivated to do so because Virgalitto et al. suggest that anti-inflammatory therapeutic actives may be employed in the film formulation and ketorolac as taught by Harrison et al. is an anti-inflammatory drug (col. 7, lines 26-67) and both Elsohly et al. and Harrison et al. are directed to vaginal formulations

Regarding claim 60, Harrison et al. teach ketorolac (= applicant's elected active species; col. 7, lines 26-67).

Regarding claim 61, the above discussions of claim 60 is incorporated by reference. Virgalitto et al. teach preferred film-forming material including, for example, cellulose polymers (e.g. hydroxypropylmethyl cellulose; para 0023), wherein the amount of said film-forming material may be from 50 to 90% by weight of the film-forming composition (para. 0027), which overlaps with the instant claim limitations. Further, Harrison et al. teach ketorolac (= applicant's elected active agent species; col. 7, lines 51-67).

Regarding claim 62, Virgalitto et al. teach chitosan as a film-forming polymer (para. 0023), which can be employed in an amount of from 50 to 90% (para. 0027). Since the instant claim also recites "chiotsan" in an amount "from about 60%, by weight," one would reasonably expect that the film compositions encompassed by the prior wherein chitosan is employed in an amount "from about 60%," by weight would also serve as a penetration enhancer as claimed. Besides, Esohly et al. teach transmucosal polymer film drug delivery systems for intra-oral and vaginal applications

(para. 0018), wherein said film matrix may optionally contain a bioadhesive such as, for example, chitosan, or others known in the art (paras. 0009 and 0019).

Regarding claim 63, Virgalitto et al. exemplify film compositions comprising polysobate 80 in an amount of 0.8%, 10%, and 1% (page 8, Examples IV-V), which overlaps with the term "wherein said surfactant is Tween 80, present in about 3%, by weight."

Regarding claim 64, the above discussion of claim 59 is incorporated by reference. The above discussion of claim 60 is incorporated by reference.

Regarding claim 65, Virgalitto et al. suggest that other components may be added to the film formulation that are commonly employed in pharmaceutical formulations (para. 0022) and Elsohly et al. teach pH buffering agents, including citric acid, sodium bicarbonate, and triethanolamine (paras. 000028-0031), which are commonly employed in pharmaceutical formulations, such that one would reasonably expect to manipulate the amount of the pH buffering agent, including arriving at applicant's claimed amounts, in order to optimize the stability of the formulation.

Regarding claim 66, the above discussion of claim 60 is incorporated by reference. As discussed above in connection with claim 59, Virgalitto et al. teach edible film that quickly hydrate and is softened and develops mucoadhesive properties, wherein thereafter said film disperses or dissolves rapidly in the oral cavity, wherein the effect of the film last for 20 minutes or more (para. 0078; see also para 0024) such that one would reasonably expect that at least 50% of the therapeutic agent to be released from the film within 80 minutes in view of the fact the edible film rapidly

disperses/dissolves when it comes in contact with body fluid (e.g. vaginal fluid). Further, since the prior art teaches every claim limitation, the prior art is considered to be capable of performing the intended function, including delivering the therapeutic agent through the epithelium into the systemic circulation as claimed.

Regarding claim 67, the above discusssions of claims 59 and 60 is incorporated by reference. Further, Elsohly et al. teach antioxidants, including BHA and BHT, to inhibit oxidation of the formulation (para. 0037) such that one would reasonably expect to add BHT to the film formulation encompassed by the prior art, as well as manipulate the amounts of the claimed components, including arriving at the instant claimed invention, in order to optimize the stability of the formulation since Virgalitto et al. suggest that other components may be added to the film formulation that are commonly employed in pharmaceutical formulations (para. 0022).

Regarding claim 68, the above discussion of 67 is incorporated by reference. Hence, one would reasonably expect to manipulate the components and the amount of components used in the formulation in order to optimize the release characteristics of the film formulation depending on the desired end use of the formulation.

Regarding claim 69, the above discussion of claim 68 is incorporated by reference.

Regarding claims 73-74, the above discussion of claim 67 is incorporated by reference.

Regarding claim 75, Elsohly et al. teach film having a diameter of 1.5 mm (para. 0042).

Thus, one would have deemed it obvious to create the instant claimed invention with reasonable predictability.

Response to applicant's arguments

Applicant's arguments with respect to the rejection under 103(a) have been considered but are moot in view of the new ground(s) of rejection. However, the merits of Elsohly et al. and Harrison et al. are maintained.

In response to applicant's argument that Elsohly et al. teach a much slower release formulation comprising THC (Figure 2) as compared to the instantly claimed ketorolac film formulation, it is the examiner's position that Virgalitto et al. state that it is desirable to provide film formulations with rapid release characteristics (para. 0008), wherein said film may comprise anti-inflammatory agents and ketorolac (= applicant's elected compound) as taught by Harrison et al. is also an anti-inflammatory agent. Further, Virgalitto et al. suggest that the release rate of the active agent from the film is dependent on the dispersibility or solubility of the film-forming polymer (para. 0024) and therefore one would reasonably expect to manipulate the release rate of the film formulation encompassed by the prior art depending on the particular properties of the active agent and the choice of the film-forming polymer or mixtures of film-forming polymers employed in the film formulation (paras. 0023-0024). Hence, applicant's assertion that Elsohly et al. teaches away from the instant claimed invention is not found to be persuasive because Virgalitto et al. state that there is a need for rapidly releasing films comprising pharmaceutical actives (e.g. anti-inflammatory agents, and various alkaloids such as morphine and codeine sulphate; paras. 0008 and 0067) and that film-

forming polymers may be employed in varying amounts depending on the nature of the film-forming polymer agent, the desired properties of the film, and the nature of the other ingredients employed in the film (para. 0027) such that one would expect to successfully manipulate the components and the amounts of the various components of the film formulation encompassed by the prior art depending on the end use of the film formulation (e.g. to treat acute dysmenorrheal).

Regarding applicant's argument that Elsohly et al. do not teach ketorolac, it is noted that the combination of references teach every claim limitation (i.e. Harrison et al. teach ketorolac; col. 7). Hence, applicant's argument is not found to be persuasive.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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12 July 2009

/C. R./ Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611